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10/652,334	08/28/2003	Stuart Peltz	54569.8003.US03	5532

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EXAMINER	
RAMIREZ, DELIA M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 02/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/652,334	PELTZ ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/8/2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,6 and 9-49* is/are pending in the application.

4a) Of the above claim(s) *5,6 and 9-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-48* is/are rejected.

7)☒ Claim(s) *49* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *8/28/2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Claims 5-6, 9-49 are pending.

Applicant's amendment of the specification, addition of claims 42-49, and cancellation of claims 7-8 in a communication filed on 11/8/2004 is acknowledged.

This application contains claims 5-6, 9-41 drawn to an invention non-elected with traverse in a communication filed on 6/28/2004 A complete reply to the final rejection must include cancellation of non-elected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

1. Claim 45 is objected to due to for not complying with sequence rules. The instant claim recites sequences for which there is no sequence identifier recited. If there is support in the specification for the sequences recited, Applicant is required to provide a sequence listing which would include the sequences recited and the claim should be amended to refer to those sequences by their sequence identifier. See particularly 37 CFR 1.821(d). Applicant is requested to make the appropriate changes.

2. Claim 42 is objected to due to the recitation of "effective to modulate peptidly transferase activity". The term "peptidly" should be replaced with "peptidyl". Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 42-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claims 42-43 (claims 44-48 dependent thereof) are indefinite in the recitation of "Upf1", "Upf2", and "Upf3" for the following reasons. In regard to a previous objection of claims 7-8 (now cancelled) due to the recitation of the term "Upf1", Applicants have indicated that the term Upf is well known in the art as it refers to proteins which are polysome-associated proteins that directly mediate the process of nonsense-mediated mRNA decay. While the Examiner acknowledges that the S. cerevisiae Upf1, Upf2, and Upf3 proteins are known in the art, and agrees that in general Upf proteins (up-frameshift) are known to mediate the process of nonsense-mediated mRNA decay, there is no indication in the specification or the art as to what is the specific function associated with any Upf1, Upf2 or Upf3 protein from any organism or the structural differences among them, such that one of skill in the art would know by recitation of the terms, what is the specific function/structure associated with each one of the Upf proteins recited. As known in the art, many proteins when first isolated are given a name which would include a general classification name followed by a numerical identifier based on the order in which they were first discover. Therefore, the different numerical identifier may not necessarily convey a specific structure and/or function beyond the general class. For examination purposes, it will be assumed that the meaning of the terms "Upf1", "Upf2", and "Upf3" is "protein that mediate the process of nonsense-mediated mRNA decay". As such, claims 43-44 will be considered duplicates of claim 42. Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 42-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s),

at the time the application was filed, had possession of the claimed invention. This rejection has been discussed at length in the Non Final Action mailed on 8/5/2004 in regard to now cancelled claims 7-8, and is now applied to new claims 42-48 for the reasons of record.

8. Applicants argue that the Written Description Guidelines do not require disclosure of what is well known or conventional in the art. Applicants refer to references by Cui et al. (Genes Dev. 9:423-436, 1995), Kisselev et al. (Biochem. Cell Biol. 73:1079-1086, 1995), and Perlick et al. (PNAS 93:10928-10932, 1996). Applicants submit that the amino acids of several eukaryotic members of the eRF1 family and eRF3 family were well known in the art at the time of filing. Regarding Upf proteins, Applicants state that Applicants have provide the yeast amino acid sequence of Upf1, a human homolog has been disclosed in the art, and that Upf2 and Upf3 from S. cerevisiae was known at the time of filing. It is Applicant's contention that because yeast is a widely accepted model for essential functions in eukaryotic cells, one would anticipate that human Upf2 and Upf3 proteins exist and would act as part of a multiprotein complex in the same way they do in S. cerevisiae. Applicants submit that many orthologs of Upf2 and Upf3 have been identified after filing of the instant application, including two human isoforms of the Upf3. Regarding Mtt1, Applicants argue that this protein was isolated from S. cerevisiae and that Applicants contemplated that there is a human Mtt1 counterpart. Also, Applicants submit that the claims also require structural features for the Mtt1 protein, specifically at least one of the motifs recited in claim 45.

9. Applicant's arguments have been fully considered but are not deemed persuasive to avoid the rejection of new claims 42-48. As indicated above, the terms "Upf1-3" have been interpreted as "protein that mediate the process of nonsense-mediated mRNA decay" in regard to claims 42-48. The Examiner acknowledges (1) the guidelines do not require disclosure of what is well known in the art, (2) the teachings of the references submitted by Applicants in response to the Non Final Action, (3) S. cerevisiae Upf1, Upf2 and Upf3 were known, (4) a human Upf1 protein has been disclosed, (5) some eRF proteins

from other organisms were known at the time of filing, (6) S. cerevisiae is commonly used as a model for essential functions in eukaryotic cells, and (7) claim 45 recite structural elements in regard to the Mtt1 protein. However, the Examiner disagrees with Applicant's contention that the genus of proteins required in the multiprotein complex is adequately described by what is disclosed in the specification and what was known in the art at the time of filing. As indicated in the previous Office Action, neither the specification nor the art provide structural features which are common to members of the genus such that a large portion of the genus is described by those structural features. While it is agreed that some species of the eukaryotic proteins recited were known in the art prior to filing of the instant application, it is noted that the claims encompass proteins whose structures are completely unknown. There is no teaching in the art or the specification which provide the structural elements in the proteins known which would also have to be present in other eukaryotic proteins to display the recited function, or the level of structural homology shared by all members of the genus. As admitted by Applicants, it is very likely that some of the recited proteins, particularly in mammals, may have more than one isoform. However, neither the specification nor the art teach how the structure of known isoforms correlate with unknown isoforms, which structural elements are present in some isoforms and not in others, or whether all the isoforms of the proteins recited when integrated in the multiprotein complex would display the recited functional characteristics.

It is reiterated herein that while a sufficient written description of a genus of polypeptides may be achieved by a recitation of a representative number of polypeptides defined by their amino acid sequence or a recitation of structural features common to members of the genus, which constitute a substantial portion of the genus, in the instant case there is no structural feature which is representative of all members of the genus of proteins recited in claims 42-44, 46-48. Also, no structural feature which is representative of eRF proteins or proteins that mediate the process of nonsense-mediated mRNA decay is recited in claim 45. In regard to the structural limitations recited for Mtt1 in claim 45, it is noted that the

claims require only one of the motifs recited. However, in view of the size of these motifs, it is unlikely that the presence of only one of these motifs is enough for a eukaryotic protein to display the desired activity. Thus, the recited structural feature in claim 45 does not constitute a substantial portion of the genus of Mtt1 proteins as the remainder of any polypeptide comprising said structural elements is completely undefined and the specification does not define the remaining structural features for members of the genus to be selected. Many structurally unrelated polypeptides are encompassed by these claims. The specification discloses a few species of the proteins required in the claimed invention, which is insufficient to put one of skill in the art in possession of the claimed invention.

10. Claims 42-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a multiprotein complex comprising the S. cerevisiae helicase B, S. cerevisiae eRF1, S. cerevisiae eRF3, S. cerevisiae Upf1p, S. cerevisiae Upf2p and S. cerevisiae Upf3p, does not reasonably provide enablement for a multiprotein complex comprising (a) any eukaryotic/yeast helicase B, (b) any eukaryotic/yeast peptidyl eukaryotic release factor 1-3, or (c) any eukaryotic/yeast protein that mediate the process of nonsense-mediated mRNA decay (Upf1, Upf2, Upf3 as interpreted), wherein the complex is able to modulate peptidyl transferase activity during translation, and wherein the complex is also able to modulate the efficiency of translation termination, or degradation of aberrant mRNA. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection has been discussed at length in the Non Final Action mailed on 8/5/2004 in regard to now cancelled claims 7-8, and is now applied to new claims 42-48 for the reasons of record.

11. Applicants argue that for the same reasons set forth in regard to the written description rejection, the scope of the claims is commensurate with the enablement provided. Applicants submit that they have provided one working example in S. cerevisiae and that there is sufficient direction in regard to an

isolated multiprotein complex including proteins isolated from a source other than yeast. Also, Applicants state that the sequences of some of the members of the genus recited where known at the time of filing and that there is a high degree of structural and functional homology among those species known in the art. Thus, Applicants conclude that the art teaches that there is a high degree of structural homology among the members of the genus and that they do share the same function.

12. Applicant's arguments have been fully considered but are not deemed persuasive to avoid the rejection of new claims 42-48. As indicated above, the terms "Upf1-3" have been interpreted as "protein that mediate the process of nonsense-mediated mRNA decay" in regard to claims 42-48. Arguments presented in regard to the written description rejection have been addressed above. The Examiner acknowledges the working example presented and agrees that some members of the genus of proteins required where known at the time of filing. However, the Examiner disagrees with Applicant's contention that the claimed invention is fully enabled by the working example provided and the structures known in the art. While it is agreed that some degree of homology exists among the species known in the art, there is no teaching in the art or the specification which would allow one of skill in the art to reasonably conclude that the same degree of homology would extend to unknown members of the genus. Furthermore, even if one were to assume that the same degree of homology is found within all members of the genus, there is no teaching in the specification or the art which would provide the structural elements that can be modified in the proteins known in the art such that homologs having that degree of homology would also display the required function. As previously indicated, the art clearly teaches that even highly structurally homologous polypeptides do not share the same function. See, particularly, the teachings of Witkowski et al., where even a single conservative substitution resulted in a different function. Therefore, use of structural homology to isolate polypeptides of similar function is unpredictable in the absence of some correlation between structure and function. Thus, for the reasons

set forth above and those of record, one cannot reasonably conclude that the claimed invention is fully enabled by the teachings of the specification.

Allowable subject matter

13. Claim 49 appears to be allowable over the prior art of record but it is objected to since it depends upon a rejected base claim.

Conclusion

14. Applicant's amendment canceling claims 7-8 and adding new claims 42-48 necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 872-9306. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be

retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

16. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
February 4, 2005

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1600~~ 1600